ORGANIC LETTERS

2009
Vol. 11, No. 11
2473−2475

One-pot Synthesis of Benzo[*b*]thiophenes and Benzo[*b*]selenophenes from *o*-Halo-Substituted Ethynylbenzenes: Convenient Approach to Mono-, Bis-, and Tris-Chalcogenophene-Annulated Benzenes

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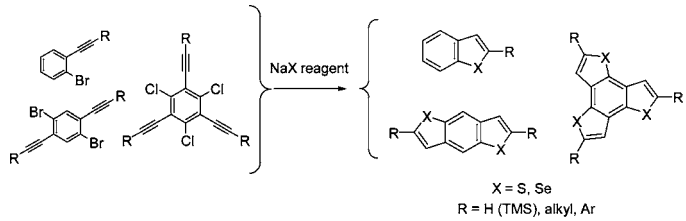
Received April 13, 2009

ABSTRACT



A convenient one-pot procedure for the synthesis of benzo[*b*]thiophenes and selenophenes from readily available *o*-halo-ethynylbenzene precursors is described. Regardless of the substituent on the acetylene terminus or the number of cyclization moieties on the precursors, various benzo[*b*]thiophenes and selenophenes, including not only the parent, alkyl-, and phenyl-substituted derivatives but also benzo[1,2-*b*:4,5-*b*′]dithiophenes and diselenophenes and benzo[1,2-*b*:3,4-*b*′:5,6-*b*″]trithiophenes and triselenophenes can be prepared in good to high yields.

Benzo[*b*]thiophene and its related derivatives represent an important class of fused-thiophene compounds in the field of bioactive materials as well as optoelectronic materials.[1] In particular, multithiophene fused-aromatic compounds are attracting current interest as promising electronic materials for organic conductors,[2] organic light-emitting diodes,[3] photovoltaic cells,[4] and field-effect transistors.[5]

For the further development of new materials based on benzo[*b*]thiophenes, it is of primary importance to devise effective synthetic methods. To this end, much work has been done to develop new and convenient synthetic approaches

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(1) (a) Zhang, T. Y.; O'Toole, J.; Proctor, C. S. *J. Sulfur Chem.* **1999**, *22*, 1–47. (b) Engel, E.; Oepen, G. In *Methoden der Organischen Chemie (Houben-Weyl)*; Kreher, R. P., Ed.; Georg Thieme Verlag: Stuttgart, NY, 1994; Vol. E6b, pp 217−274.

(2) (a) Wudl, F.; Haddon, R. C.; Zellers, E. T.; Bramwell, F. B. *J. Org. Chem.* **1979**, *44*, 2491–2493. (b) Takimiya, K.; Yashiki, F.; Aso, Y.; Otsubo, T.; Ogura, F. *Chem. Lett.* **1993**, 365–367. (c) Takimiya, K.; Otsubo, T.; Ogura, F. *J. Chem. Soc., Chem. Commun.* **1994**, 1859–1860. (d) Takimiya, K.; Kato, K.; Aso, Y.; Ogura, F.; Otsubo, T. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 1795–1805.

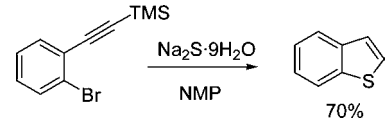
10.1021/ol900809w CCC: $40.75
Published on Web 05/11/2009

to benzo[*b*]thiophenes. In particular, the use of phenylacetylene-based precursors in cyclization reactions affording fused-thiophene or selenophene moieties has emerged: Sashida et al. reported that *o*-alkynylbromobenzenes react with elemental chalcogene (sulfur, selenium, or tellurium) upon lithium−halogen exchange to afford benzo[*b*]chalcogenophenes in good yields.[6] On the other hand, Larock and co-workers employed *o*-alkynyl-thioanisole or -selenoanisole in the electrophilic cyclization reaction to give benzo[*b*]-thiophenes and -selenophenes, respectively, where *o*-methylthio or methylseleno groups are an excellent chalcogen source.[7] The superiority of these new methods was proved by the high yields of the desired products, the tolerance for various substituents, and successful applications to 2-fold cyclization reactions to give benzo[1,2-*b*:4,5-*b*′]dithiophenes and benzo-[1,2-*b*:5,4-*b*′]diselenophenes.[8]

During the course of our synthetic studies on heteroaromatic compounds for use as electronic materials,[9] we have pursued efficient methods to introduce sulfur functional groups to aromatic rings and have focused on inorganic sulfur sources, such as sodium sulfide (Na_2S), in the aromatic nucleophilic substitution (S_NAr) reaction. To our knowledge, very limited examples of the syntheses of benzo[*b*]thiophenes using such inorganic reagents have been reported: Shvartsberg and co-workers reported the thiophene-annulation reaction of 2-alkynyl-1-chloro- and 1-alkynyl-2-chloroanthraquinones with Na_2S to yield anthra[1,2-*b*]thiophene-6,11-diones and anthra[2,1-*b*]thiophene-6,11-diones, respectively.[10] In the reactions, electron-withdrawing anthraquinone moieties in the substrates activate the initial substitution reaction of Na_2S with the substrate.

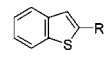
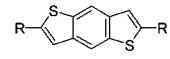
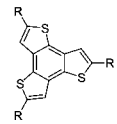
For nonactivated substrates without strong electron-withdrawing groups, the S_NAr reactions of sulfur-based nucleophiles can be accelerated by use of polar aprotic solvents and/or by elevating the reaction temperature.[11] We thus examined a similar cyclization reaction using Na_2S as reagent and 1-bromo-2-trimethylsilylethynylbenzenes as substrates in *N*-methyl-2-pyrrolidone (NMP) at 180 °C (Scheme 1). After usual workup, unsubstituted benzo[*b*]thiophene was obtained in 70% isolated yield as the major product. This indicates that Na_2S acts as a nucleophile to nonactivated bromobenzenes and the resulting phenylthiolate intermediate attacks the adjacent acetylene moiety to form the thiophene ring. Although the trimethylsilyl (TMS) group was displaced during the reaction, probably due to the high basicity of the reagent, we recognized that this one-pot procedure for the synthesis of benzo[*b*]thiophene is very useful because various kinds of precursors, not only *o*-alkynylbromobenzenes with different substituents at the acetylene terminus but also the potential precursors for benzo[1,2-*b*:4,5-*b*′]dithiophenes (BDTs) and benzo[1,2-*b*:3,4-*b*′:5,6-*b*″]trithiophenes (BTTs), are easily available.

Scheme 1. Reaction of 1-Bromo-2-trimethylsilylethynylbenzene with Na_2S



We thus carried out the reactions of *n*-hexyl- and phenyl-substituted *o*-ethynylbromobenzenes under the same reaction conditions (Table 1). As expected, corresponding 2-*n*-hexyl- and 2-phenyl-benzo[*b*]thiophenes were isolated in high yields. Similarly, 2-fold cyclization using 1,4-dibromo-2,5-bis(alkenyl)benzenes was examined. Dihexyl- and diphenyl-

Table 1. Synthesis of Benzo[*b*]thiophenes, benzo[1,2-*b*:4,5-*b*′]dithiophenes, and Benzo[1,2-*b*:3,4-*b*′:5,6-*b*″]trithiophenes

	yield[a] / %		
	TMS (H)[b]	C_6H_{13}	Ph
	70	82	73
	88	68	57[c]
	62	62	75

[a] Isolated yields after purification by column chromatography and/or recrystallization. [b] Trimethylsilyl group(s) were removed during the reaction to give the parent benzo[*b*]thiophenes. Purified by vacuum gradient sublimation.

(3) (a) Mazzeo, M.; Vitale, V.; Sala, F. D.; Pisignano, D.; Anni, M.; Barbarella, G.; Favaretto, L.; Zanelli, A.; Cingolani, R.; Gigli, G. *Adv. Mater.* **2003**, *15*, 2060–2063. (b) Huang, T.-H.; Lin, J. T.; Chen, L. Y.; Lin, Y. T.; Wu, C. C. *Adv. Mater.* **2006**, *18*, 602–606.

(4) Bettignies, R. d.; Nicolas, Y.; Blanchard, P.; Levillain, E.; Nunzi, J. M.; Roncali, J. *Adv. Mater.* **2003**, *15*, 1939–1943.

(5) (a) Laquindanum, G. L.; Katz, H. E.; Lovinger, A. J.; Dodabalapur, A. *Adv. Mater.* **1997**, *9*, 36–39. (b) Sirringhaus, H.; Friend, R. H.; Wang, C.; Leuningerb, J.; Müllen, K. *J. Mater. Chem.* **1999**, *9*, 2095–2101. (c) Laquindanum, J. G.; Katz, H. E.; Lovinger, A. J. *J. Am. Chem. Soc.* **1998**, *120*, 664–672. (d) Takimiya, K.; Kunugi, Y.; Konda, Y.; Niihara, N.; Otsubo, T. *J. Am. Chem. Soc.* **2004**, *126*, 5084–5085. (e) Takimiya, K.; Kunugi, Y.; Toyoshima, Y.; Otsubo, T. *J. Am. Chem. Soc.* **2005**, *127*, 3605–3612. (f) Payne, M. M.; Parkin, S. R.; Anthony, J. E.; Kuo, C. C.; Jackson, T. N. *J. Am. Chem. Soc.* **2005**, *127*, 4986–4987. (g) Ebata, H.; Miyazaki, E.; Yamamoto, T.; Takimiya, K. *Org. Lett.* **2007**, *9*, 4499–4502. (h) Ebata, H.; Izawa, T.; Miyazaki, E.; Takimiya, K.; Ikeda, M.; Kuwabara, H.; Yui, T. *J. Am. Chem. Soc.* **2007**, *129*, 15732–15733. (i) Takimiya, K.; Ebata, H.; Sakamoto, K.; Izawa, T.; Otsubo, T.; Kunugi, Y. *J. Am. Chem. Soc.* **2006**, *128*, 12604–12605. (j) Yamamoto, T.; Takimiya, K. *J. Am. Chem. Soc.* **2007**, *129*, 2224–2225. (k) Gao, J.; Li, R.; Li, L.; Meng, Q.; Jiang, H.; Li, H.; Hu, W. *Adv. Mater.* **2007**, *19*, 3008–3011.

(6) Sashida, H.; Sadamori, K.; Tsuchiya, T. *Synth. Commun.* **1998**, *28*, 713–727.

(7) (a) Yue, D.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 1905–1909. (b) Yue, D.; Yao, T.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 10292–10296.

(8) (a) Takimiya, K.; Konda, Y.; Ebata, H.; Niihara, N.; Otsubo, T. *J. Org. Chem.* **2005**, *70*, 10569–10571. (b) Wang, C.-H.; Hu, R.-R.; Liang, S.; Chen, J.-H.; Yang, Z.; Pei, J. *Tetrahedron Lett.* **2005**, *46*, 8153–8157. (c) Takimiya, K.; Konda, Y.; Ebata, H.; Otsubo, T.; Kunugi, Y. *Mol. Cryst. Liq. Cryst.* **2006**, *455*, 361–365.

(9) Takimiya, K.; Kunugi, Y.; Otsubo, T. *Chem. Lett.* **2007**, *36*, 578–583.

(10) Ivanchikova, I. D.; Lebedeva, N. I.; Shvartsberg, M. S. *Synthesis* **2004**, 2131–2134.

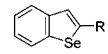
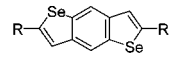
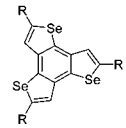
substituted precursors gave the corresponding disubstituted BDTs in reasonable yields, whereas the TMS-substituted one gave the parent BDT in 88% isolated yield (Table 1). For the synthesis of BTTs, 1,3,5-trichloro-2,4,6-tris(alkenyl)benzenes[12] instead of the corresponding tribromobenzene were used because of the ready availability of the former. Even with the trichloride precursors, the reactions proceeded smoothly to give corresponding BTTs; i.e., the parent, trihexyl-, and triphenyl-BTTs were obtained in reasonable isolated yields (Table 1).

Three-fold cyclization on the benzene ring to afford BTTs has not been attainable so far even with the recently developed benzo[*b*]thiophene syntheses[6,7] due to the lack of suitable precursors and/or the difficulty of generating synthetic intermediates. Therefore, BTTs were prepared by a multistep synthesis using expensive starting materials and tedious reactions including the oxidative photoinduced cyclization reaction.[13] The present direct synthesis of BTTs from easily available precursors will pave the way to the chemistry of these intriguing heteroarenes with C_{3h} symmetry.[4,13,14]

In order to extend the present strategy to the synthesis of benzo[*b*]selenophenes, we examined similar reactions of the *o*-halo-ethynylbenzene precursors with sodium selenide reagents that were generated in situ from sodium borohydride ($NaBH_4$) and selenium powder in ethanol. The results of the synthesis of benzo[*b*]selenophenes, benzo[1,2-*b*:4,5-*b*′]diselenophenes (BDSs), and benzo[1,2-*b*:3,4-*b*′:5,6-*b*″]triselenophenes (BTSs) are summarized in Table 2. Similar to the syntheses of benzo[*b*]thiophenes, selenophene cyclization on the benzene ring took place smoothly regardless of the substituent on the acetylene terminus or the number of cyclization moieties on the precursors to give various benzo[*b*]selenophene derivatives in reasonable to good yields. In particular, the first successful synthesis of BTSs should be noted.[15]

In summary, we have successfully established a convenient one-pot procedure for the synthesis of benzo[*b*]thiophenes and benzo[*b*]selenophenes from *o*-halo-substituted ethynylbenzenes using sodium chalcogenides as reagents. Owing to the accessibility of the precursors, the easy experimental operation, and the reasonable yields of the products, the present method for the synthesis will be beneficial for developing new materials based on benzo[*b*]thiophenes and benzo[*b*]selenophenes. In particular, the applicability to the 3-fold cyclization on the benzene ring affords straightforward access to benzo[1,2-*b*:3,4-*b*′:5,6-*b*″]-trithiophenes and -triselenophenes, which are hitherto very tedious to synthesize or not synthesizable. Using these heteroarene structures, the development of new optoelectronic materials is now being actively pursued.

Table 2. Synthesis of Benzo[*b*]selenophenes, Benzo[1,2-*b*:4,5-*b*′]diselenophenes, and Benzo[1,2-*b*:3,4-*b*′:5,6-*b*″]triselenophenes

	yield[a] / %		
	TMS (H)[b]	C_6H_{13}	Ph
	77	81	73
	68	87	52[c]
	60	80	81

[a] Isolated yields after purification by column chromatography and/or recrystallization. [b] Trimethylsilyl group(s) were removed during the reaction to give the parent benzo[*b*]thiophenes. [c] Purified by vacuum gradient sublimation.

Acknowledgment. This work was partially supported by a Grant-in-Aid for Scientific Research (No. 20350088) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Supporting Information Available: Experimental details for the synthesis and characterization of benzo[*b*]-thiophenes and -selenophenes; X-ray crystallographic file (CIF). These materials are available free of charge via the Internet at http://pubs.acs.org.

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(11) (a) Cogolli, P.; Maiolo, F.; Testaferri, L.; Tingoli, M.; Tiecco, M. *J. Org. Chem.* **1979**, *44*, 2642–2646. (b) Shaw, J. E *J. Org. Chem.* **1991**, *56*, 3728–3729.

(12) Sonoda, M.; Inaba, A.; Itahashi, K.; Tobe, Y. *Org. Lett.* **2001**, *3*, 2419–2421.

(13) (a) Proetzsch, R.; Bieniek, D.; Korte, F. *Tetrahedron Lett.* **1972**, *13*, 543–544. (b) Jayasuriya, N.; Kagan, J.; Owens, J. E.; Kornak, E. P.; Perrine, D. M. *J. Org. Chem.* **1989**, *54*, 4203–4205. (c) Nicolas, Y.; Blanchard, P.; Levillain, E.; Allain, M.; Mercier, N.; Roncali, J. *Org. Lett.* **2004**, *6*, 273–276.

(14) Roncali, J.; Leriche, P.; Cravino, A. *Adv. Mater.* **2007**, *19*, 2045–2060.

(15) All new compounds were characterized by spectroscopic and combustion analyses. The structure of the parent benzo[1,2-*b*:3,4-*b*′:5,6-*b*″]triselenophene was also confirmed by X-ray structural analysis. See Supporting Information for details.